September 25, 2008

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Article courtesy of Dave Wehrly, Chair, Central Beryllium IRB

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from Heartwire — a professional news service of WebMD

ENROLLMENT STOPPED IN NIH-FUNDED TRIAL STUDYING CHELATION THERAPY FOR TREATMENT OF CAD

September 25, 2008 (updated September 26, 2008) (Miami, FL) — Enrollment into the Trial to Assess Chelation Therapy (TACT), a five-year, $30-million National Institutes of Health (NIH)--funded clinical study, has been stopped.

"The investigators and institutions performing the trial, in conjunction with their institutional review boards [IRBs], have temporarily and voluntarily suspended enrollment of new participants in the study," Susan Dambrauskas, a media officer at the National Heart, Lung, and Blood Institute (NHLBI), a cosponsor of the study, wrote in an email to heartwire.

The American College for Advancement in Medicine (ACAM), an organization that promotes findings and emerging procedures in complementary, alternative, and integrative medicine, issued a statement about the stoppage, but with it raised the possibility of wrongful conduct [1].

According to the statement, ACAM supports the NIH's decision to suspend patient accrual of TACT "until allegations of impropriety can be proven false." It goes on to state the allegations are "of a political nature" before calling for a swift end to the moratorium and resumption of the trial.

Speaking with heartwire, lead TACT investigator Dr Gervasio Lamas (University of Miami Miller School of Medicine, FL) said the Office for Human Research Protections (OHRP) received a complaint from an outside party about the consent process for patient enrollment in the trial. There were concerns raised that the consent form was incomplete, as well as safety concerns raised about the therapy, Asked for specifics, Lamas would not disclose the exact nature of the complaint, saying the issue is currently under review with the IRBs as requested by the OHRP.

"If the OHRP has these questions, we need to really look at everything in the most serious way possible," said Lamas. "While we do that and while we consult with our own IRB regarding the consent form, it would be best to temporarily stop enrolling new patients. The deliberation is ongoing. We're working with the University of

Miami IRB, which is the parent IRB for the study, and we expect an answer about the study as it's designed."

TACT: A Controversial Study Called Wasteful, Pointless, and Dangerou s

TACT is a randomized, double-blind, placebo-controlled study evaluating the efficacy of ethylene-diamine-tetra-acetic acid (EDTA) chelation therapy in the treatment of coronary artery disease. Patients 50 years of age and older who have had a prior MI have been randomly assigned to receive 40 infusions of the standard chelation solution or placebo.

The primary end point of the trial is a composite of all-cause mortality, MI, stroke, hospitalization for angina, and hospitalization for congestive heart failure. Enrollment was estimated at around 2000 patients, and the trial was to be completed in July 2009. So far, 1500 patients have been enrolled and 22 000 injections of EDTA been given.

There is skepticism, however, in the medical community about the safety and efficacy of chelation therapy. While TACT was designed to definitively answer the question about the potential benefit of using chelation to treat coronary artery disease, the trial itself has become a lightning rod for criticism.

In a peer-reviewed article appearing May 13, 2008 in the Medscape Journal of Medicine [2], Dr Kimball Atwood (Newton-Wellesley Hospital, MA) and colleagues wrote: "The TACT is pointless, dangerous, unethical, and a waste of public funds. It should be stopped immediately and permanently, and its origin and nature subjected to an independent, comprehensive inquiry."

In the article, Atwood, who is an associate editor of the Scientific Review of Alternative Medicine, writes that chelation poses risks for patients and that the evidence against its use should disqualify it from further clinical trials. Atwood said the trial exists only because political pressure willed it into existence.

The review goes on to state that the application for the trial misrepresented previous data and concealed evidence of risks, as well as lacked precautions to minimize that risk. The consent form, according to Atwood et al, reflects these shortcomings. Moreover, they say, the trial is flawed because the consent form fails to disclose financial information--particularly, that some investigators profit from chelation therapy.

"There is little basis for predicting that the TACT will yield a reliable or definitive result and even less for predicting a favorable effect on clinical practice," according to Atwood and colleagues. "Numerous coinvestigators are unfit to care for subjects in a human trial or to submit trustworthy information to the NIH."

Lamas said the investigators are sensitive to the criticisms and take the issues raised by the Medscape Journal of Medicine article seriously. When the review was published, the TACT investigators convened several conference calls to discuss the

issues raised but felt there was no need to make any changes to the study or the consent form and continued with the trial. After the issue went to the OHRP, they decided to voluntarily suspend=2 0enrollment to address these concerns for a second time.

"All of us take it very seriously and if our IRB says the consent form has to change, it will change," said Lamas. The data safety and monitoring board, he added, last met in April 2008, a point when approximately 20 000 active-therapy infusions had been given, and no safety concerns were raised.

"When you get a respected federal agency involved, you really need to step back and say, 'Am I really providing the best patient protection and patient information that I can?' " said Lamas. "And I'm happy to do that. The purpose of this is never to carry out research in a way where research is not valid or people are unhappy. The primary purpose in any of these research studies has to be to maintain patient safety."

Chelation therapy has been used since 1955 for the treatment of coronary artery disease. Agents such as EDTA, which bind metals and are approved by the FDA to treat heavy-metal poisoning, are given intravenously to decalcify atherosclerotic plaque. Proponents of the therapy, led by ACAM, which has issued a protocol for chelation therapy, reason that this therapy may alter plaque morphology and volume or improve endothelial function.

The National Center for Complementary and Alternative Medicine (NCCAM) is also a study sponsor.

The Medscape Journal of Medicine is an open-access peer-reviewed general medic al journal available on Medscape. Medscape is owned by WebMD, which also owns theheart.org.

American College for Advancement in Medicine. ACAM supports NIH decision to suspend TACT trial [press release]. September 3, 2008. Available at: www.acamnet.org

Atwood KC, Woeckner E, Baratz RS, Sampson WI. Why the NIH Trial to Assess Chelation Therapy (TACT) should be abandoned. Medscape J Med 2008; 10:115. Abstract

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